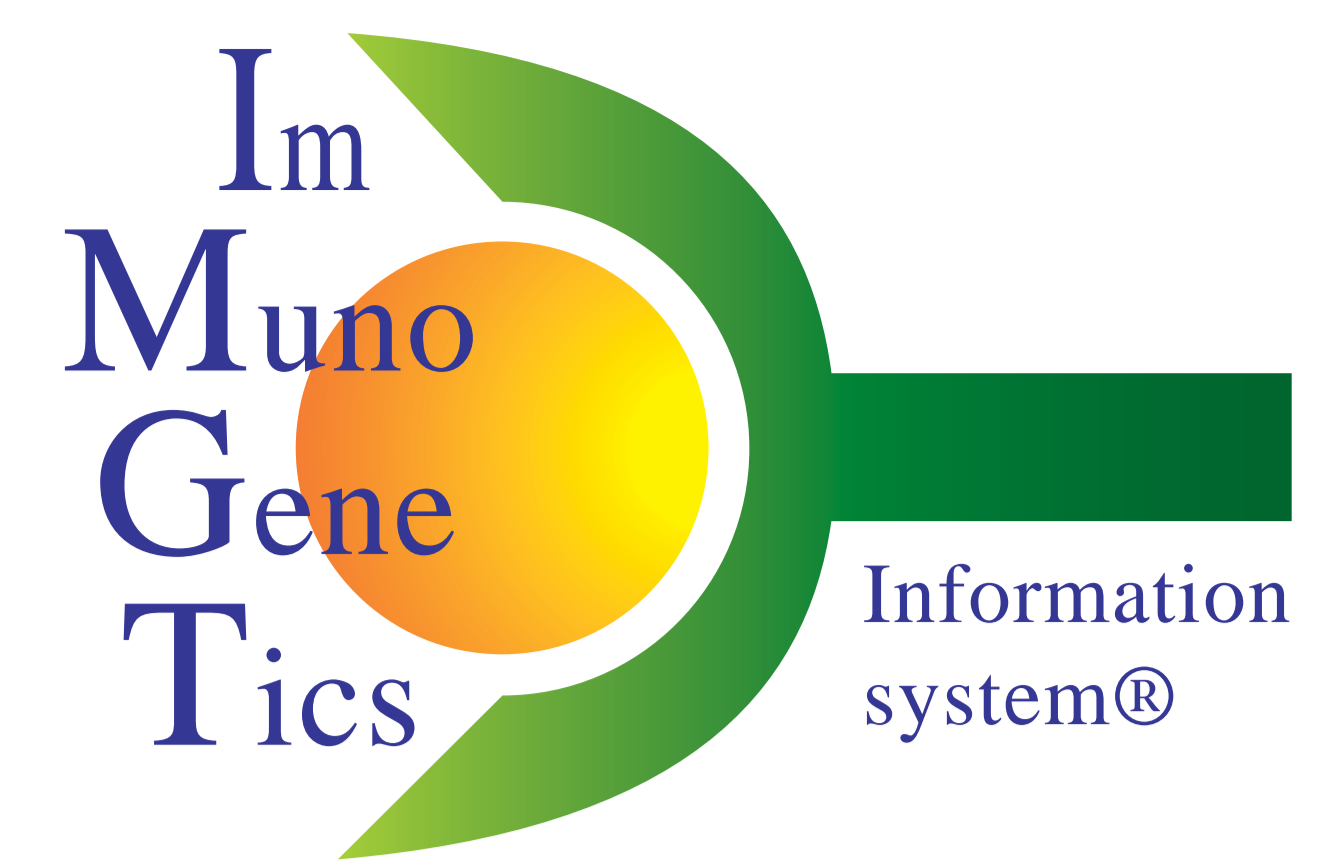# IMGT/3Dstructure-DB and tools for immunoglobulins (IG) or antibodies, T cell receptors (TR), MHC, IgSF and MhcSF structural data

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Im Muno Gene Tics
Information system®
http://www.imgt.org

IMGT®, the international ImMunoGeneTics information system®, provides a three-dimensional (3D) structure database (IMGT/3Dstructure-DB) and tools for sequences and structures analysis (IMGT/DomainDisplay, IMGT/DomainGapAlign and IMGT/Collier-de-Perles). IMGT/3Dstructure-DB data are annotated according to the IMGT® criteria, using IMGT/DomainGapAlign, and based on the IMGT-ONTOLOGY concepts and axioms. IMGT/3Dstructure-DB provides IMGT gene and allele identification (CLASSIFICATION), region and domain delimitations (DESCRIPTION), amino acid positions according to the IMGT unique numbering (NUMEROTATION). Coupled to the IMGT/Collier-de-Perles tool, IMGT/3Dstructure-DB and IMGT/DomainGapAlign provide an invaluable help for antibody engineering and humanization design based on complementarity determining regions (CDR).

Ehrenmann F., Kaas Q. and Lefranc M.-P. Nucleic Acids Res 38: D301-307 (2010)
Kaas Q., Ruiz M. and Lefranc M.-P. Nucleic Acids Res. 32: D208-210 (2004)
Lefranc M.-P. et al Nucleic Acids Res. 37: 1006-1012 (2009)
Kaas Q., Ehrenmann F. and Lefranc M.-P. Brief. Funct. Genomic Proteomic, 6:253-264 (2007)
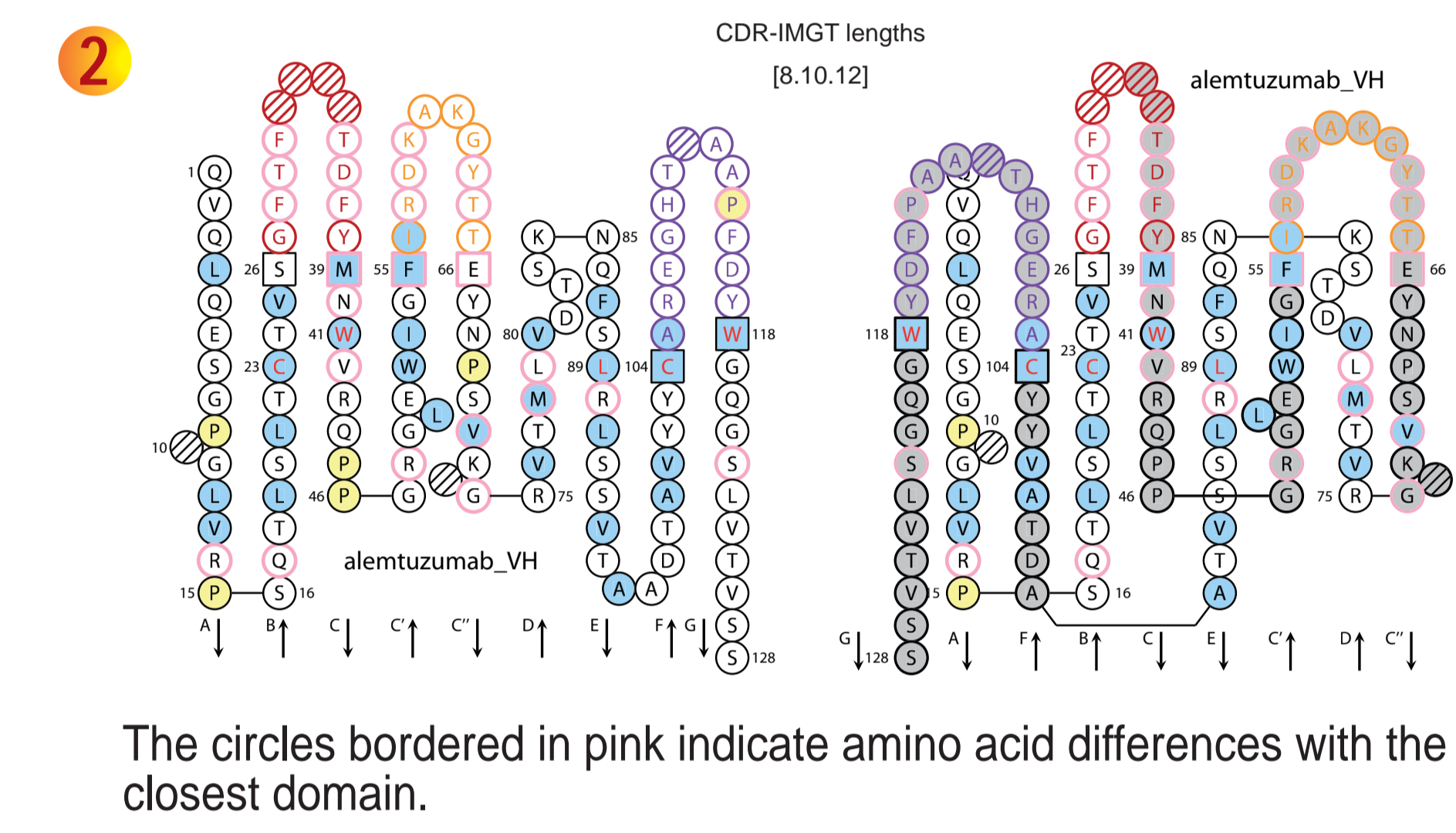
IMGT/DomainGapAlign

Amino acid sequences are analysed per domain using the IMGT/DomainGapAlign tool. Several sequences of the same domain type (V, C or G) may be analysed simultaneously.

IMGT/DomainGapAlign identifies the closest germline V-REGION (for 'V'), C-DOMAIN (for 'C') or G-DOMAIN (for 'G'), creates gaps according to the IMGT unique numbering and highlights differences with the closest reference(s). For an antibody V domain sequence, the tool identifies the closest germline V-REGION and J-REGION, and provides a delimitation of the strands, framework regions (FR-IMGT) and CDR-IMGT. The gene and allele name of the closest sequence(s) from the IMGT domain directory is provided with a percentage of identity and a Smith-Waterman score. Regions and domains are highlighted using the IMGT color menu and IMGT Colliers de Perles are generated from the gapped sequences provided by the tool.
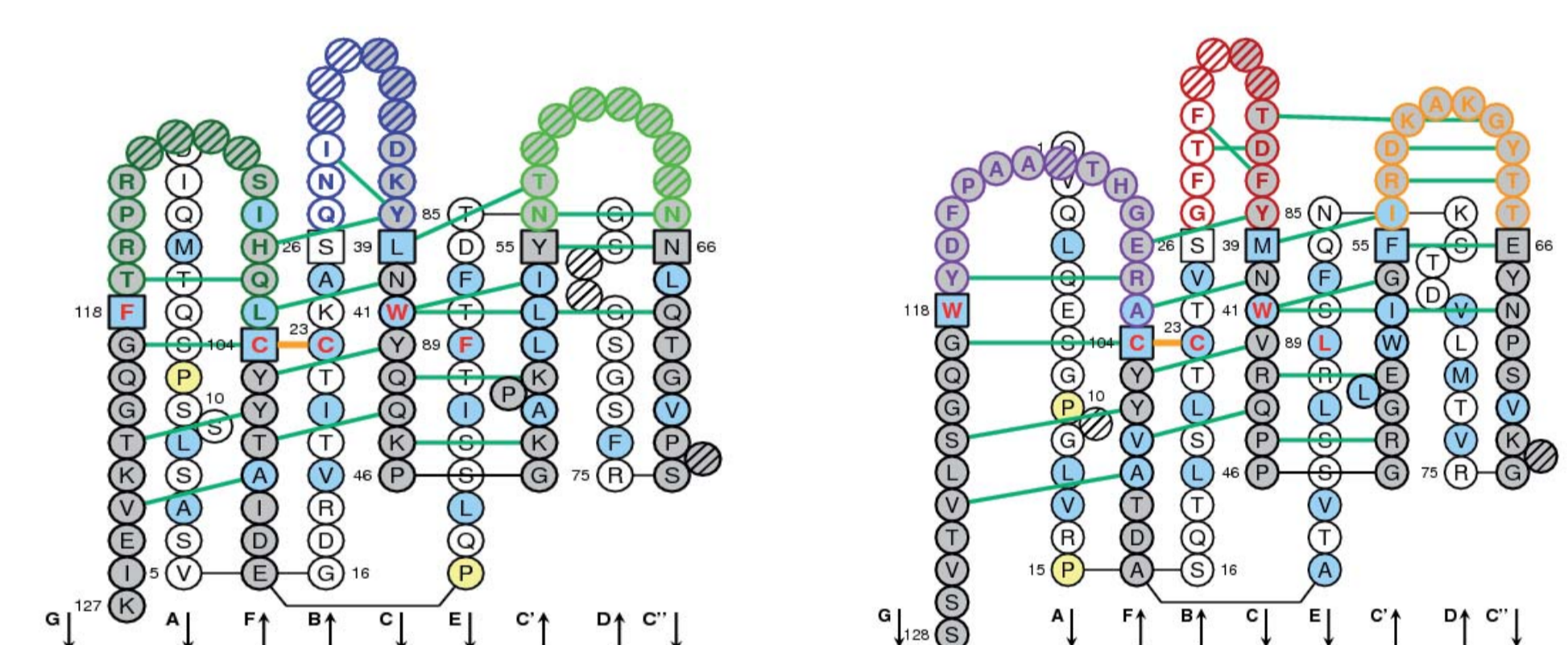
The circles bordered in pink indicate amino acid differences with the closest domain.

IMGT/3Dstructure-DB
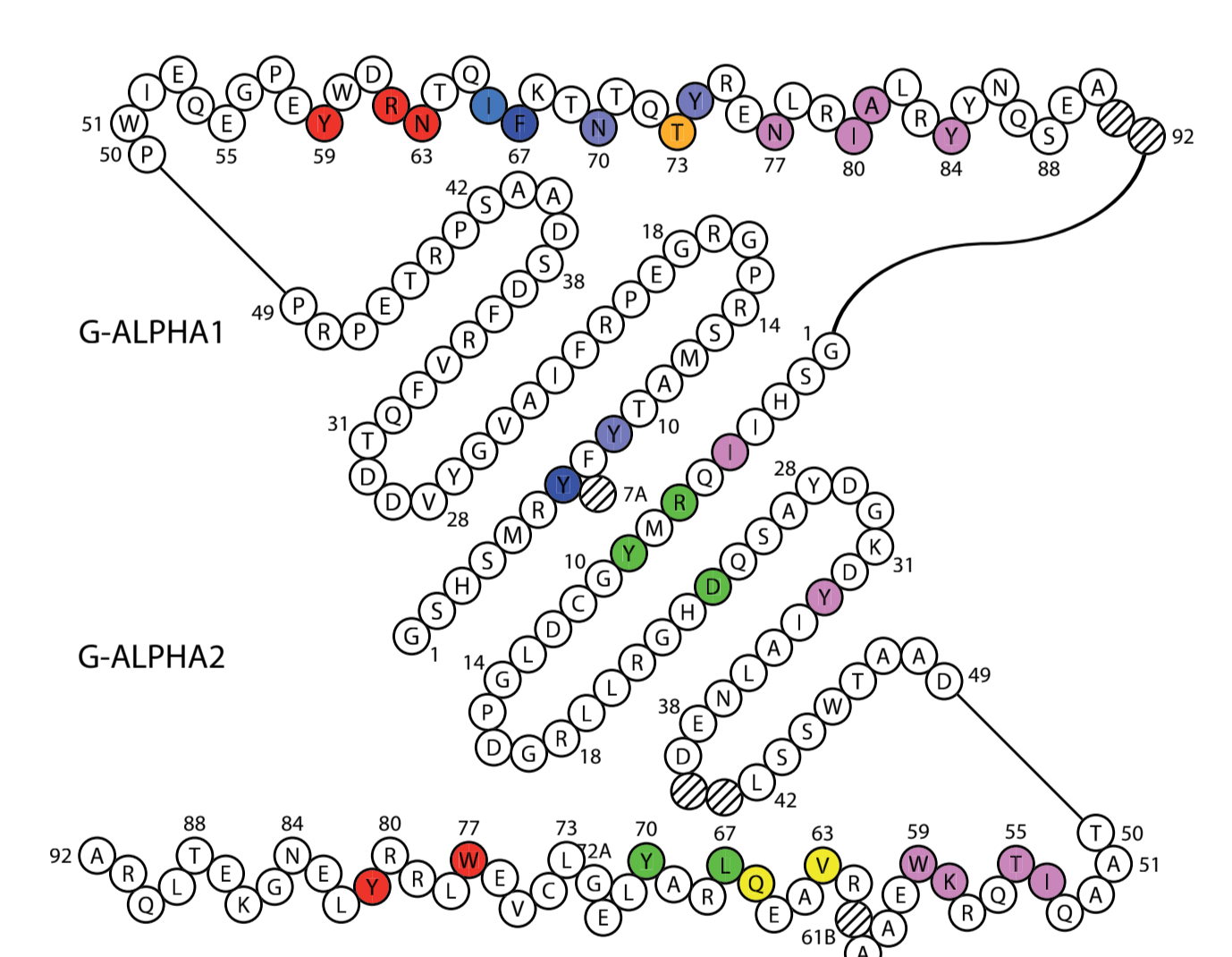
IMGT/3Dstructure-DB card

If one 3D structure is available (for example 1ce1 for alemtuzumab), it is possible to query IMGT/3Dstructure-DB:
- to visualize **hydrogen bounds** in the IMGT Collier de Perles on two layers
- to check the **contact analysis** table. This table provides contacts between structural units (domains or ligand).

IMGT pMHC contact sites graphically represent, in IMGT Colliers de Perles, the MHC amino acid positions that contact the peptide side chains in pMHC complexes, and thus allow comparison of pMHC interactions.

Ehrenmann F., Kaas Q. and Lefranc M.-P. Nucleic Acids Res. 38: D301-307 (2010)

IMGT/Collier-de-Perles

Make your own IMGT Collier de Perles

IMGT/Colliers de Perles are 2D graphical representations available for the V type domain, C type domain and groove (G) type domain. Any domain represented by an IMGT Collier de Perles is characterized by the length of its strands, loops and turns and, for the G type, by the length of its helix. IMGT Colliers de Perles are generated with the IMGT/Collier-de-Perles tool which allows the users to draw Colliers de Perles starting from their own amino acid sequences. Sequences have to be gapped according to the IMGT unique numbering, using for example IMGT/DomainGapAlign.

Using the IMGT/Collier-de-Perles tool, IMGT Colliers de Perles can be displayed:
- on one or two layers
- with the VH or VL coloring of the CDR-IMGT
- with the IMGT amino acid physicochemical classes for the FR-IMGT. This allows to evaluate the number of IMGT amino acid class changes.

Pommié C. et al. J. Mol. Recognit. 17:17-32 (2004)

FR-IMGT and antibody humanization

A standardized comparison of V domain sequences for antibody humanization includes the delimitation of the FR-IMGT and CDR-IMGT, the determination of the CDR-IMGT lengths (e.g. [8.8.13]), the percentage of identity between FR-IMGT [calculated on 91 amino acids for VH (FR1-, FR2-, FR3-, FR4-IMGT: 25, 17, 38, 11) and 89 for V-KAPPA (FR1-, FR2-, FR3-, FR4-IMGT: 26, 17, 36, 10)] and the number of IMGT amino acid physicochemical class changes.

Humanized antibodies used in oncology

	Humanized antibody	CDR-IMGT antibody	Closest *Homo sapiens* gene and allele	FR-IMGT identity	AA with IMGT class change in FR-IMGT
VH	alemtuzumab	[8.10.12]	IGHV4-59*01	84.61% (77/91)	14
	bevacizumab	[8.8.16]	IGHV7-4-1*02	74.72% (68/91)	24
	trastuzumab	[8.8.13]	IGHV3-66*01	90.10% (82/91)	9
VL	alemtuzumab	[6.3.9]	IGKV1-33*01	97.75% (87/89)	2
	bevacizumab	[6.3.9]	IGKV1-33*01	92.13% (82/89)	7
	trastuzumab	[6.3.9]	IGKV1-39*01	93.25% (83/89)	5

Note that the use of the IMGT unique numbering would enable to reach 100% for the FR-IMGT identity. Although a few positions need to be checked for antibody humanization such as 39 and 40 (FR2-IMGT) as then interact with CDR2-IMGT and CDR3-IMGT, respectively.

Magdaleine-Beuzelin C. et al. Crit. Rev. Oncol. Hematol. 64:210-225 (2007)

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